Inhaled drug therapy for the management of asthma

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There is a wide range of inhaler devices to choose from for asthma. This drug review highlights their advantages and disadvantages as well as the importance of inhaler technique.

Asthma is a chronic inflammatory disease of the airways characterised by reversible airflow obstruction. Over five million people in the UK suffer with asthma and the healthcare burden of the disease is significant. Asthma guidelines encourage a ‘step-up’ approach in pharmacological treatment to achieve disease control and a ‘step-down’ strategy when asthma is under control. In this strategy, inhaled drug therapy remains the foundation in managing patients with asthma. This review highlights the range of inhaler devices used for asthma, their advantages and disadvantages and the importance of inhaler technique. The advantages and disadvantages of the common inhaler devices are shown in Table 1 and online videos of inhaler use are also available.

Inhaled drug delivery

Inhalation has long been established as an effective way to deliver drug to the lungs to manage respiratory diseases. Compared to oral tablets, inhaled medicines are delivered directly to the airways and allow a smaller dose to be administered leading to a quicker onset of action and fewer side-effects. A range of devices is used to deliver inhaled drug. These include pressurised metered-dose inhalers (pMDIs), spacers, dry-powder inhalers (DPIs) and nebulisers.

There are various factors that affect lung deposition of medical aerosols. These are summarised in Table 2.

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Disadvantages</th>
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| **Pressurised metered-dose inhaler (pMDI)** | Difficulty in hand-mouth co-ordination  
Oropharyngeal deposition may be high  
Older device propellants may cause ‘cold Freon’ effect and affect climate change  
Usually no dose counter to assess empty canister |
| Compact and portable  
Drug in sealed canister  
Multi-dose  
Inexpensive  
Quick treatment time |
| **Soft-mist inhaler (SMI)** | Requires some co-ordination of actuation and inhalation  
Slightly heavier than pMDI, DPI |
| Dose counter  
Portable and quick dose delivery  
‘Soft mist’ moves slowly and low inhalation flows needed |
| **Dry powder inhaler (DPI)** | High oropharyngeal deposition  
Humidity can cause drug degradation  
Need adequate inhalation flow to disperse drug  
Patients may be intolerant to additives, eg lactose |
| Breath actuation removes need for co-ordination  
Compact and portable  
Quick treatment time |
| **Nebulisers** | Bulky, cumbersome and expensive  
Need for power source  
Regular cleaning and maintenance  
Time consuming  
Variation in aerosol output performance between models  
Wasted drug in nebuliser reservoir |
| Aerosolise many drug solutions  
Large doses of drug can be given  
Suitable for young, old and acutely ill patients  
Use with relaxed tidal breathing |

Table 1. Advantages and disadvantages of inhaler devices

**Pressurised metered-dose inhalers**

pMDIs contain the drug mixed with a propellant, usually hydrofluoroalkane (HFA), in a sealed canister. pMDIs no longer contain the ozone-depleting chlorofluorocarbon (CFC) propellants and are either HFA-solution or HFA-suspension devices. HFA-solution pMDIs have a smaller drug particle size and achieve greater lung deposition than HFA-suspension pMDIs which have a larger drug particle size. The recommended inhalation technique from a pMDI is to comfortably breathe out, place the inhaler in the mouth...
Inhaler devices

<table>
<thead>
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<th>Aerosol characteristics</th>
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<td>Drug particle size</td>
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<td>Plume speed duration</td>
<td>Device acceptance</td>
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<td>adherence</td>
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Table 2. Factors influencing the deposition of medical aerosols in the lung

between the lips, then actuate at the start of a deep breath and undertake a slow inhalation lasting for five seconds, followed by a breath-hold pause of ten seconds. A deep and slow inhalation avoids drug depositing in the throat, as on actuation of the pMDI canister the drug spray is forced out at a high velocity. In contrast, HFA-solution pMDIs have a spray that is slower and data show that these devices achieve less deposition in the oropharynx compared to DPIs.

Prim ing the pMDI inhaler is necessary and refers to the number of test sprays that should be actuated when the inhaler is being used for the first time or after a long interval of time. Different pMDIs have different priming instructions. Patient co-ordination between inhalation and actuation can be a problem with pMDIs especially in elderly patients with difficulties in manual dexterity and handling. Add-on spacer attachments and breath-actuated pMDIs have been developed to overcome this. Breath-actuated MDIs are triggered by the patient’s inspiratory force, but do not offer an advantage over pMDIs for those patients with good co-ordinated pMDI inhaler technique.

Spacers

Spacer devices are an extension attachment to the pMDI device and simply provide a ‘space’ and distance between the patient’s mouth and the inhaler device to slow down the high velocity of the emitted aerosol cloud. This leads to reduced throat deposition and allows time for greater evaporation of the propellant, leading to relatively smaller drug particles that have greater potential to deposit within the lungs. For dosing requiring more than one actuation, a single dose actuation at-a-time from the pMDI into the spacer device should be used. The patient should inhale each dose, rather than sequential multiple-dose administrations. A Cochrane review has shown that in the emergency scenario, spacer attachments with pMDIs are as effective as nebulisers in the management of patients with asthma exacerbations.

It is important to appreciate that there are many spacers each differing in their design and spacers should be prescribed only with the pMDI they are compatible with. British Thoracic Society guidelines recommend spacers should be washed in mild detergent and allowed to air dry every month, and replaced at least every 12 months if not 6 months. One consideration is that electrostatic charge on the walls of plastic spacers can decrease the amount of drug that will be deposited in the lungs. However, new non-electrostatic and anti-static spacers have been developed that prevent medication from sticking to the sides of the spacer, but these are more expensive.

Soft mist inhalers

As with HFA-solution pMDIs, soft-mist inhalers (SMIs) have been developed that have a slow-moving aerosol spray and smaller particle size. There is therefore less potential for local side-effects (eg oral candidiasis from corticosteroids) and for systemic absorption by swallowing the dose.

Dry powder inhalers

DPIs are propellant-free and usually contain powdered drug particles that are bound to larger carrier molecules such as lactose. The efficacy of DPIs is highly dependent on the patient’s inspiratory effort. High inhalation flows (sometimes as high as 60L/min) are needed to de-aggregate the drug from the lactose carrier molecule and achieve optimal drug delivery to the lungs. Indeed, studies have observed that patients with asthma and those with chronic obstructive pulmonary disease often use inadequate inhalation flows from DPIs and this can lead to low levels of drug delivery to the lungs. Of concern is a patient’s ability to achieve an adequate inspiratory effort to use a DPI during a respiratory exacerbation, where a high respiratory rate may significantly compromise drug delivery.

DPIs come in a variety of devices. Single-dose delivery systems include those that require individual drug capsules to be manually loaded into the inhaler prior to use, and those where individual doses are dispensed from punctured gelatine capsules. Multiple-dosing DPIs avoid the inconvenience associated with constant loading of the drug and can be ‘multi-dose’ devices that deliver metered-drug from a powder reservoir, and ‘multi-unit-dose’ devices where drug is sealed in individual foil blisters or in pockets on a moving strip.

DPIs vary in their instructions for use, particularly in loading the drug-device prior to inhalation. In general the patient should comfortably breathe out, hold the inhaler in the correct position, place the inhaler in the mouth between the lips and then inhale deep and fast followed by a breath-hold pause of ten seconds (in most devices). The recommendation for a deep and fast inhalation is to de-aggregate the drug, but a good proportion of the drug from a DPI deposits in the oropharynx.

Factors to consider when choosing between individual DPIs to adequately deliver the drug to the patient include: the need to be held in the correct position; not blowing into the device/mouthpiece prior to inhalation; and some capsule devices requiring more than one inhalation. DPIs should be stored in a dry environment as the drug may deteriorate in damp and humid conditions (such as the bathroom cabinet). Newer DPIs have recently been developed that do not rely so critically on the patient’s inspiratory effort, needing gentler and slower inhalation flows than conventional DPI devices to achieve optimal drug delivery to the lungs.

Nebuliser

Ultrasonic and jet nebulisers are those commonly used in clinical practice. Ultrasonic nebulisers work by using high
frequency vibrations directed at the drug liquid in order to generate aerosol clouds for inhalation. Jet nebulisers use high velocity pressurised air directed through a narrow Venturi opening over the surface of the drug liquid to produce aerosols for inhalation within the nebulising chamber. Ultrasonic nebulisers are smaller and less noisy compared to jet nebulisers, but are usually less robust, more expensive and not as effective in nebulising liquid suspensions of drug. Generally, compared with conventional pMDI and DPI inhalers, nebuliser devices lack portability, are large and have longer treatment times.

The recommended inhalation technique from nebulisers requires comfortable tidal breathing and there is little need for patient co-ordination. Attention should be given to the nebuliser/face-mask combination and its correct insertion to avoid drug depositing on the face and eyes, especially in children. However, between the many devices there are great differences in the aerosol output, and the inhalation manoeuvres being used by the patient will affect drug delivery to the lungs; for example, crying or shallow and rapid inhalations can decrease the amount of drug delivered to the lungs. New nebuliser devices have been developed that allow an improvement in the amount of drug reaching the lungs. Some of these devices pulse the drug only during the inspiratory phase, thereby decreasing drug loss that occurs during exhalation. New systems also allow an assessment of patient compliance with treatment and provide feedback to the patient. Although these devices are more costly compared with conventional nebulisers, overall they may be cost-effective by more effectively delivering a reduced drug dose to the lungs and by minimising loss of drug from the nebuliser chamber during exhalation.

Putting it into practice
There is a range of inhaler devices with differing treatments, each requiring a different set of instructions for use and this can lead to confusion and ‘device dementia’ among healthcare professionals. Healthcare professionals need good education in the correct use of inhaler devices and so do patients, as they may misunderstand device-specific instructions resulting in improper administration technique and impaired drug delivery.

• Don’t change a patient’s inhaler device without engaging with them.
• Assess the patient’s ability (inhalation effort and dexterity) to use the device.
• Reassess inhaler technique at every opportunity.
• Keep things simple – try to prescribe one ‘type’ of device for the range of medications.

References

Declaration of interests
None to declare.

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